

**Biographical Sketch:****Robert Charles LADNER**, PhD

Senior Vice President and Chief Technical Officer, Dyax Corp.

**Education:**

Rice University	B.A.	1966	Chemistry
CalTech	PhD	1972	Theoretical Chemistry

**Postdoctoral Training**

1972	Centre European de Calcul Atomique et Moleculaire, Computational Chemistry
1973-1976	Medical Research Council Laboratory of Molecular Biology, X-ray Crystallography

**Employment**

1976-1979	European Molecular Biology Laboratory, Computer Molecular Modeling
1979-1983	Harvard U., Research Associate, Computer Molecular Modeling
1983-1987	Genex Corp. Computer Molecular Modeling and Theoretical Molecular Biology
1987-1995	Protein Engineering Corporation, Founder, Chief Scientist
1995-2003	Dyax Corp., Chief Scientific Officer, Sr. V. P.
2003-now	Dyax Corp., Chief Technical Officer, Sr. V. P.

**Selected Publications:**

1. Markland, W., Roberts, B.L., Saxena, M.J., Guterman, S.K., Ladner, R.C. (1991) *Gene* **109**(1)13-9. "Design, construction and function of a multicopy display vector using fusions to the major coat protein of bacteriophage M13."
2. Roberts, B. L., Markland, W., Ley, A. C., Kent, R. B., White, D. W., Guterman, S. K., Ladner, R. C. Directed evolution of a protein: selection of potent neutrophil elastase inhibitors displayed on M13 fusion phage. *Proc Natl Acad Sci U S A* (1992) **89**(6)2429-33.
3. Roberts, B.L., Markland, W., Siranosian, K., Saxena, M.J., Guterman, S.K., Ladner, R.C. (1992) *Gene* **121**(1)9-15. "Protease inhibitor display M13 phage: selection of high-affinity neutrophil elastase inhibitors".
4. McLafferty, M.A., Kent, R.B. Ladner, R.C., Markland, W. (1993) *Gene* **128**(1)29-36. "M13 bacteriophage displaying disulfide-constrained microproteins".
5. Ladner, R. C., Guterman S. K., Roberts B. L., Markland, W., Ley, A. C., Kent, R. B. Directed evolution of novel binding proteins. US Patent 5,223,409; 1993.
6. Ladner, R. C. Constrained peptides as binding entities. (1995) *Trends Biotechnol* **13**(10):426-30.
7. Markland, W., Ley, A. C., Lee, S. W., Ladner, R. C. Iterative optimization of high-affinity proteases inhibitors using phage display. 1. Plasmin. *Biochemistry* **35**(24):8045-57, 1996.
8. Markland, W., Ley, A. C., Ladner, R. C. Iterative optimization of high-affinity protease inhibitors using phage display. 2. Plasma kallikrein and thrombin. *Biochemistry* **35**(24):8058-67, 1996.
9. Ley, A.C., Markland, W., Ladner, R.C. (1996) *Mol Divers* **2**(1-2)119-24. "Obtaining a family of high-affinity, high-specificity protein inhibitors of plasmin and plasma kallikrein"
10. Roberts, B.L., Markland, W., Ladner, R.C. (1996) *Methods Enzymol* **267**:68-82. "Affinity maturation of proteins displayed on surface of M13 bacteriophage as major coat protein fusions".
11. Markland, W., Roberts, B.L., Ladner, R.C. (1996) *Methods Enzymol* **267**:28-51. "Selection for protease inhibitors using bacteriophage display".
12. Ladner, R.C. "Display and Selection of Proteins on Genetic Packages." Chapter 10 in **Phage Display of Peptides and Proteins: A Laboratory Manual**. Edited by B.K. Kay, J. Winter, J. McCafferty. Academic Press, San Diego, 1996.

13. Hnatowich, D.J., Qu, T., Chang, F., Ley, A.C., Ladner, R.C., Rusckowski, M. (1998) *J Nucl Med* **39**(1)56-64. "Labeling peptides with technetium-99m using a bifunctional chelator of a N-hydroxysuccinimide ester of mercaptoacetyltryglycine"
14. Larocca D, Kassner PD, Witte A, Ladner RC, Pierce GF, Baird A (1999) *FASEB J* **13**(6)727-34. "Gene transfer to mammalian cells using genetically targeted filamentous bacteriophage."
15. Ladner, R.C. (1999) *Q J Nucl Med* **43**(2)119-24. "Polypeptides from phage display. A superior source of in vivo imaging agents."
16. Rusckowski M, Qu T, Pullman J, Marcel R, Ley AC, Ladner RC, Hnatowich DJ (2000) *J Nucl Med* **41**(2)363-74. "Inflammation and infection imaging with a 99mTc-neutrophil elastase inhibitor in monkeys."
17. Ladner, R.C. (2000) *Pharmacogenomics* **1**(2)199-202. "Phage display and pharmacogenomics".
18. Ladner RC, Ley AC. (2001) *Curr Opin Biotechnol.* **12**(4)406-410. "Novel frameworks as a source of high-affinity ligands."
19. Sato AK, Sexton DJ, Morganelli LA, Cohen EH, Wu QL, Conley GP, Streltsova Z, Lee SW, Devlin M, DeOliveira DB, Enright J, Kent RB, Wescott CR, Ransohoff TC, Ley AC, Ladner RC. (2002) *Biotechnol Prog.* **18**(2)182-192. "Development of mammalian serum albumin affinity purification media by peptide phage display."
20. Huang L, Sexton DJ, Skogerson K, Devlin M, Smith R, Sanyal I, Parry T, Kent R, Enright J, Wu QL, Conley G, DeOliveira D, Morganelli L, Ducar M, Wescott CR, Ladner RC. (2003) *J Biol Chem.* **278**(18)15532-15540. "Novel peptide inhibitors of angiotensin-converting enzyme 2."
21. van den Beucken T, Pieters H, Steukers M, van der Vaart M, Ladner RC, Hoogenboom HR, Hufton SE. (2003) *FEBS Lett.* **546**(2-3)288-294. "Affinity maturation of Fab antibody fragments by fluorescent-activated cell sorting of yeast-displayed libraries."
22. Ladner RC, Sato AK, Gorzelany J, de Souza M. (2004) *Drug Discov Today.* **9**(12)525-9. "Phage display-derived peptides as therapeutic alternatives to antibodies."
23. Kelley BD, Booth J, Tannatt M, Wub QL, Ladner R, Yuc J, Potter D, Ley A. (2004) *J Chromatogr A.* **1038**(1-2)121-30. "Isolation of a peptide ligand for affinity purification of factor VIII using phage display."
24. Hoet RM, Cohen EH, Kent RB, Rookey K, Schoonbroodt S, Hogan S, Rem L, Frans N, Daukandt M, Pieters H, van Hegelsom R, Neer NC, Nastri HG, Rondon IJ, Leeds JA, Hufton SE, Huang L, Kashin I, Devlin M, Kuang G, Steukers M, Viswanathan M, Nixon AE, Sexton DJ, Hoogenboom HR, Ladner RC. (2005) *Nat Biotechnol.* **23**(3)344-8. "Generation of high-affinity human antibodies by combining donor-derived and synthetic complementarity-determining-region diversity."
25. Hogan S, Rookey K, Ladner R. (2005) *Biotechniques.* **38**(4)536, 538. "URSA: ultra rapid selection of antibodies from an antibody phage display library."
26. Schoonbroodt S, Frans N, DeSouza M, Eren R, Priel S, Brosh N, Ben-Porath J, Zauberman A, Ilan E, Dagan S, Cohen EH, Hoogenboom HR, Ladner RC, Hoet RM. (2005) *Nucleic Acids Res.* **33**(9)e81. "Oligonucleotide-assisted cleavage and ligation: a novel directional DNA cloning technology to capture cDNAs. Application in the construction of a human immune antibody phage-display library."
27. Shrivastava A, von Wronski MA, Sato AK, Dransfield DT, Sexton D, Bogdan N, Pillai R, Nanjappan P, Song B, Marinelli E, DeOliveira D, Luneau C, Devlin M, Muruganandam A, Abujoub A, Connelly G, Wu QL, Conley G, Chang Q, Tweedle MF, Ladner RC, Swenson RE, Nunn AD.

- (2005) *Protein Eng Des Sel*. **18**(9)417-24. "A distinct strategy to generate high-affinity peptide binders to receptor tyrosine kinases."
28. Wassaf D, Kuang G, Kopacz K, Wu QL, Nguyen Q, Toews M, Cosic J, Jacques J, Wiltshire S, Lambert J, Pazmany CC, Hogan S, Ladner RC, Nixon AE, Sexton DJ. (2006) *Anal Biochem*. **351**(2)241-53. "High-throughput affinity ranking of antibodies using surface plasmon resonance microarrays."
29. Huang L, Shimaoka M, Rondon IJ, Roy I, Chang Q, Po M, Dransfield DT, Ladner RC, Edge AS, Salas A, Wood CR, Springer TA, Cohen EH. (2006) *J Leukoc Biol*. **80**(4)905-14. "Identification and characterization of a human monoclonal antagonistic antibody AL-57 that preferentially binds the high-affinity form of lymphocyte function-associated antigen-1."
30. Ladner RC. (2007) *Nat Biotech*. **25**(8)875-7. "Antibodies cut down to size."
31. Devy L, Rabbani SA, Stochl M, Ruskowski M, Mackie I, Naa L, Toews M, van Gool R, Chen J, Ley A, Ladner RC, Dransfield DT, Henderikx P. (2007) *Neoplasia*. **9**(11)927-37. "PEGylated DX-1000: pharmacokinetics and antineoplastic activity of a specific plasmin inhibitor."
32. Ladner RC. (2007) *Biotechnol Genet Eng Rev*. **24**:1-30. "Mapping the epitopes of antibodies."
33. Buckler DR, Park A, Viswanathan M, Hoet RM, Ladner RC. (2008) *Drug Discov Today* **13**(7-8)318-24. "Screening isolates from antibody phage-display libraries."
34. Schoonbroodt S, Steukers M, Viswanathan M, Frans N, Timmermans M, Wehnert A, Nguyen M, Ladner RC, Hoet RM. (2008) *J Immunol*. **181**(9)6213-21. "Engineering antibody heavy chain CDR3 to create a phage display Fab library rich in antibodies that bind charged carbohydrates."
35. Devy L, Huang L, Naa L, Yanamandra N, Pieters H, Frans N, Chang E, Tao Q, Vanhove M, Lejeune A, van Gool R, Sexton DJ, Kuang G, Rank D, Hogan S, Pazmany C, Ma YL, Schoonbroodt S, Nixon AE, Ladner RC, Hoet R, Henderikx P, Tenhoor C, Rabbani SA, Valentino ML, Wood CR, Dransfield DT. (2009) *Cancer Res*. **69**:1517-26. Epub 2009 Feb 10.

Patents (I have listed only the US patent except in cases for which there is no US patent corresponding to a European patent)

#### Single-chain antibodies:

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|-----|--------------|------------|
| 1)  | US 5,534,621 | 1996.07.09 |
| 2)  | US 5,518,889 | 1996.05.21 |
| 3)  | US 5,455,030 | 1995.10.03 |
| 4)  | US 5,260,203 | 1993.11.09 |
| 5)  | US 4,946,778 | 1990.08.07 |
| 6)  | EP 349,578   | 1990.02.28 |
| 7)  | US 4,881,175 | 1989.11.14 |
| 8)  | US 4,853,871 | 1989.08.01 |
| 9)  | US 4,908,773 | 1990.03.13 |
| 10) | US 4,704,692 | 1987.11.03 |

#### Phage Display:

1)	US 7,514,534	2009.04.07
2)	US 7,438,890	2008.10.21
3)	US 7,413,537	2008.08.19
4)	US 7,329,737	2008.02.12
5)	US 7,276,480	2007.10.02
6)	US 7,244,592	2007.07.17
7)	US 7,235,530	2007.06.26
8)	US 7,208,293	2007.04.24
9)	US 7,153,829	2006.12.26
10)	US 7,118,879	2006.10.10
11)	US 7,118,872	2006.10.10
12)	US 7,078,383	2006.07.18
13)	US 7,074,560	2006.07.11
14)	US 7,064,107	2006.06.20
15)	US 6,989,369	2006.01.24
16)	US 6,979,538	2005.12.27
17)	US 6,953,674	2005.10.11
18)	US 6,919,424	2005.07.19
19)	US 6,906,176	2005.06.14
20)	US 6,744,209	2004.08.10
21)	US 6,462,172	2002.10.08
22)	US 6,423,498	2002.07.23
23)	US 6,333,402	2001.12.25
24)	US 6,326,155	2001.12.04
25)	US 6,103,499	2000.08.15
26)	US 6,084,062	2000.07.04
27)	US 6,071,723	2000.06.06
28)	US 6,057,287	2000.05.02
29)	US 6,010,880	2000.01.04
30)	US 5,994,125	1999.11.30
31)	US 5,837,500	1998.11.17
32)	US 5,795,865	1998.08.18
33)	US 5,663,143	1997.09.02
34)	US 5,571,698	1996.11.05
35)	US 5,403,484	1995.04.04
36)	US 5,223,409	1993.06.29
37)	EP 349,578	1990.02.28

## Other patents:

1)	US 7,550,427	2009.06.23
2)	US 7,514,534	2009.04.07
3)	US 5,198,346	1993.03.30

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4) US 5,096,815 1992.03.17